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Patent
Attorney Docket No. AUG 30 2003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

TECH CENTER 1600/2900

In re Patent Application of

Larry S. BARAK et al.

Application No.: 10/054,616

Filing Date: January 22, 2002

Title: Constitutively Desensitized G Protein-Coupled Receptors

Group Art Unit: 1645

Examiner: Unassigned

Confirmation No.: 7096

**THIRD
INFORMATION DISCLOSURE STATEMENT
TRANSMITTAL LETTER**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Enclosed is a **THIRD** Information Disclosure Statement and accompanying form PTO-1449 for the above-identified patent application.

- ☒ No additional fee for submission of an IDS is required.
- ☐ The fee of \$180.00 (1806) as set forth in 37 C.F.R. § 1.17(p) is also enclosed.
- ☐ A statement under 37 C.F.R. § 1.97(e) is also enclosed.
- ☐ A statement under 37 C.F.R. § 1.97(e), and the fee of \$180.00 (1806) as set forth in 37 C.F.R. § 1.17(p) are also enclosed.
- ☐ Charge _____ to Deposit Account No. 02-4800 for the fee due.
- ☐ A check in the amount of _____ is enclosed for the fee due.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

P.O. Box 1404
Alexandria, Virginia 22313-1404
(919) 941-9240

Date: 8/19/03

By Allen R. Baum
Allen R. Baum
Registration No. 36,086



Attorney's Docket No. 033072-022

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Larry S. BARAK et al.

Application No.: 10/054,616

Filed: January 22, 2002

For: Constitutively Desensitized G Protein-Coupled Receptors

Group Art Unit: 1645

Examiner: Unassigned

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TECH CENTER 1600/2900

THIRD INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure as set forth in 37 C.F.R. § 1.56, Applicants hereby submit the following information in conformance with 37 C.F.R. §§ 1.97 and 1.98.

Pursuant to 37 C.F.R. § 1.98, a copy of each of the documents cited is enclosed.

Enclosed is a copy of an International Search Report, prepared in the corresponding International application. The documents are being submitted within three (3) months of the filing or entry of the national stage of this application or before the first Office Action on the merits, whichever is later. Since these documents are being filed within the time period set forth in 37 C.F.R. § 1.97(b), no fee or statement is required.

To assist the Examiner, the document is listed on the attached form PTO-1449. It is respectfully requested that an Examiner initialed copy of this form be returned to the undersigned.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: Allen R. Baum
Allen R. Baum
Registration No. 36,086

P.O. Box 1404
Alexandria, Virginia 22313-1404
(919) 941-9240

Date: 8/20/03

(use as many sheets as necessary)

1

of

1

Attorney Docket Number	033072-022
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[illegible][illegible]

Examiner Initials	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
	ALEWIJNSE, ASTRID E., et al., <i>The Effect of Mutations in the DRY Motif on the Constitutive Activity and Structural Instability of the Histamine H₂ Receptor</i> , <u>Molecular Pharmacology</u> , 2000, pp. 890-898, 57, American Society for Pharmacology & Experimental Therapeutics, 0026-895X/00/050890, Baltimore, MD

Date
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with M.P.E.P. § 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

PATENT COOPERATION TREATY

HKB/SMC
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
RECEIVED

MAY - 6 2003

PCT

DOCKETED

From the INTERNATIONAL SEARCHING AUTHORITY

To:
ALLEN R. BAUM
BURNS, DOANE, SWECKER AND MATHIS, L.L.P.
P.O. BOX 1404
ALEXANDRIA, UT 22313-1404

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

MAY 09 2003

Applicant's or agent's file reference
033072-057

Date of Mailing
(day/month/year)

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US02/01701 ✓

International filing date
(day/month/year)

23 January 2002 (23.01.2002)

Applicant
DUKE UNIVERSITY

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34, chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 bis.1 and 90 bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US
Commissioner for Patents
Box PCT
Washington, D.C. 20231
Facsimile No. (703)305-3230

Authorized officer

Helicia D. Robert for
Michael Pak

Telephone No. 703-308-1235

Form PCT/ISA/220 (April 2002)

(See notes on accompanying sheet)

DOCKETED

Article 19 Amendment due
7-2-03

Prof
5.1.03

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
ALLEN R. BAUM
BURNS, DOANE, SWECKER AND MATHIS, L.L.P.
P.O. BOX 1404
ALEXANDRIA, UT 22313-1404

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 033072-057	Date of Mailing (day/month/year) 02 MAY 2003
International application No. PCT/US02/01701	International filing date (day/month/year) 23 January 2002 (23.01.2002)
Applicant DUKE UNIVERSITY	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34, chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

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Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Commissioner for Patents Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer <i>Michael Pak</i> Michael Pak Telephone No. 703-308-1235
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Form PCT/ISA/220 (April 2002)

(See notes on accompanying sheet)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 033072-057	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US02/01701	International filing date (<i>day/month/year</i>) 23 January 2002 (23.01.2002)	(Earliest) Priority Date (<i>day/month/year</i>) 23 January 2001 (23.01.2001)
Applicant DUKE UNIVERSITY		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (See Box II).

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. _____



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/01701

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claim Nos.: 1-17,28-30,32 and 33
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
The claims require sequence search and the sequence was not in compliance.
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐

The additional search fees were accompanied by the applicant's protest.

☐

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/01701

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 14/705, 16/00; C12N 5/10, 15/00, 15/09, 15/12, 15/63; G01N 33/53
US CL : 435/7.2, 320.1, 325; 530/350, 387.1; 536/23.5; 800/2

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/7.2, 320.1, 325; 530/350, 387.1; 536/23.5; 800/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ALEWJINSE et al. The effect of mutations in the DRY motif on the constitutive activity and structural instability of the histamine H2 receptor. Molecular Pharmacology. May 2000, Vol. 57, pages 890-898.	18-27, 31, 34-38

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

24 April 2003 (24.04.2003)

Date of mailing of the international search report

02 MAY 2003

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Melissa D. Roberts for
Michael Pak

Telephone No. 703-308-1235

INTERNATIONAL SEARCH REPORT

PCT/US02/01701

Continuation of B. FIELDS SEARCHED Item 3:
BRS, STN, MEDLINE

search terms: g-protein coupled receptor, mutagenesis, constitutive desensitization

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.